

# **Pesticide Epidemiology in US EPA's Office of Pesticide Programs**

## **Update and Current Activities**

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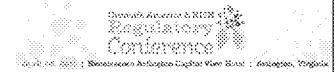
Director, Health Effects Division  
Office of Pesticide Programs  
U.S. Environmental Protection Agency

*CLA/RISE Regulatory Conference, Spring 2019*

*Session on: Good Epidemiology Practices for Pesticide Exposure Assessment*

Renaissance Hotel, Arlington VA

**4 April 2019**



# Outline

- EPA/OPP Regulatory Mandate
- Epidemiological Studies in EPA/OPP
- EPA/OPP Approach: Tiered Process
- Other or Ongoing Epidemiological Projects/  
Activities

# EPA Regulatory Mandate

- US EPA's Office of Pesticide Programs (OPP) is the US governmental agency responsible for registering and regulating pesticide products in the USA.
  - As part of this activity, OPP evaluates the effects of pesticides on human health and the environment.
- Under FIFRA and FQPA, EPA has a regulatory mandate to determine if pesticides cause unreasonable adverse effects on human health.
  - OPP receives extensive hazard and exposure information through FIFRA and FFDCA.
  - Information on hazard generally derived from laboratory animal studies.
  - High quality, pesticide-specific epidemiological information has not traditionally been widely available.

# Epidemiological Studies in OPP

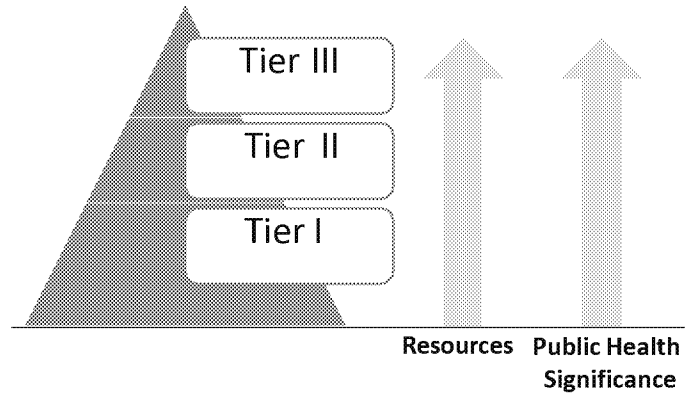
- An increasing number of epidemiology studies are entering literature, particularly from the Agricultural Health Study (AHS) and its publications.
- OPP is putting increasing emphasis and the use of these epidemiology studies in its Human Health Risk Assessments.
  - Goal is to use this information in a scientifically robust and transparent way.
- Epidemiology review is an important component of the risk assessment process and complements other information available to the Agency.

# Epidemiology Assessment Approach

- Tiered reviews are guided by OPP's Epidemiological Framework published in 2016
- Emphasizes study quality and weight of evidence
- "Fit for purpose"
  - Required resources are "matched" or balanced against any anticipated or expected information gain from further, more in-depth research
  - Can include formal systematic review, when appropriate
    - Systematic review: *"a scientific investigation that focuses on a specific question and uses explicit, pre-specified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies"*
    - US EPA IRIS, NTP/OHAT, "Navigation Guide" (EHP series)

# Tiered Review Approach

- EPA's Office of Pesticide Programs has adopted a tiered assessment approach to fulfill its regulatory mandate and respond to emerging public health issues.
  - Manage program workload
  - Prioritize potential risk issues that warrant systematic investigation



## Tier I, Tier II, & Tier III Epidemiology Reviews

- **Tier I: Update to scoping exercise**
  - Research and evaluation generally limited to Agriculture Health Study (AHS)-related publications
- **Tier II: Systematic review**
  - Broader search of epidemiologic literature including comprehensive data collection and systematic literature review
  - Generally limited in scope to epidemiology
  - Integration by risk assessors occurs as part of Draft Risk Assessment
- **Tier III: Systematic review + multi-disciplinary integration**
  - Can involve more comprehensive epidemiologic methods
    - Meta-analysis; Design calculations/power issues; Publication; Bias/Egger (Funnel) Plots; Multiple Comparisons/False Discovery Rate; Heterogeneity/  $I^2$ ; Meta-regression; Sensitivity analysis/quantitative bias analysis; Causal Analysis



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# Tier I, Tier II, & Tier III Epidemiology Reviews

## Links to Tier I Epi/incident reviews available in the chemical dockets:

- ***Captan***: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2013-0296-0045>
- *Trifluralin*: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0417-0022>
- ***Bromoxynil***: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0896-0023>
- ***Imazethapyr***: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2013-0774-0022>
- Carbaryl: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2010-0230-0035>
- EPTC: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0720-0017>
- Aldicarb: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0161-0024>

## Links to Tier II Epi/incident reviews available in the chemical dockets:

- ***Atrazine***: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2013-0266-1156>
- Diazinon: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0351-0091>
- Permethrin: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0039-0084>
- 2,4-D: <https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0330-0084> for carcinogenic effects and <https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0330-0087> for non-carcinogenic effects.

***Bold italics*** = newest ones in docket



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# Other Epidemiological Projects/Activities

- HESI (Health and Environmental Sciences Institute)
  - Series of small focus group sessions with tripartite representation from regulators, industry, and academia in a dialogue on the use of environmental epidemiology for regulatory decision-making [more, next- C.Chen...]
- IRAC (Interagency Risk Assessment Consortium)
  - Multi-agency workgroup within IRAC co-chaired by FDA/CBER and EPA/OPP exploring regulatory issues associated with epidemiology studies as they relate to reproducibility and replication
  - Effect size magnification/design calculations; quantitative bias analysis (QBA); Reproducibility and Replication Benefits and Challenges
- International Society of Environmental Epidemiology (ISEE)

Annual Meeting is August 2020 in Washington, D.C

# Summary

- OPP has placed increased emphasis on incorporating high quality epidemiology studies, when available, in its Human Health Risk Assessments, with the goal of using this information in a scientifically robust and transparent way.
- Review of epidemiologic research is an important component of the EPA OPP risk assessment process mandated under FIFRA and FQPA.
- In order to support regulatory risk assessment and public interest needs, OPP has adopted a tiered review approach to manage workload and prioritize potential risk issues that warrant systematic investigation
- OPP is involved in variety of other collaborative epidemiological activities